which are expected to relax very fast. A further support to the assignment and to the whole interpretation of the relaxation properties of the system comes from the evaluation of τ_c for these protons. In fact, assuming a cobalt–H4 distance of 530 pm as found in a model complex,[32] a τ_c of 3.5×10^{-12} is calculated from the Solomon–Bloembergen equation, which is in fair agreement with the value determined from the various magnetic field measurements on the water protons.

The spectra recorded in H_2O show evidence of two further protons whose signals fall at –60 and –46 ppm (Figure 2), which can be safely assigned to the NH protons in position 3.[22] Upon comparison of the present spectra with those of five-coordinated derivatives of cobalt carbonic anhydrase,[22] it appears that the signals of the present system are broader, although the τ_c values of the two systems are rather close. Perhaps the high concentration of NaCl, necessary to dissolve CPA, contributes to the line width; furthermore, the large flexibility of the active cavity[33] may allow movements of the coordinated histidines with an exchange time of the order of the difference in chemical shift among the various positions. Such mechanism would account for the large line width observed. A similar justification was given for the failure to observe an NMR signal from ^{113}Cd in the cadmium(II) deriva-

tive.[34] In the case of the NH groups, the chemical exchange through hydrogen bonds with water in the cavity may be another source of line broadening.

In conclusion, measurements at various magnetic fields of the water ^1H T_1^{-1} of solutions containing CoCPA and the inhibitor β-phenylpropionate have provided an electronic correlation time supporting the hypothesis of a five-coordinated chromophore. The geometrical parameters deduced through the Solomon–Bloembergen equation suggest the presence of two water molecules, which would complete the coordination sphere together with the protein ligands, two histidines, and one glutamate residue. The inhibitor substitutes a water molecule, leaving the coordination number unaltered.

In the ^1H NMR spectra of the protein part a significantly larger line width with respect to what would have been expected from the T_1 values and from the comparison with analogous systems[22,35] has been attributed to some conformational interactions whose justification stems on the large flexibility of the system.

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Communications to the Editor

A Synthetic Isorhodopsin Formed with a Retinal Derivative Lacking an Intact Ring

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The photosensitive pigment of the vertebrate retina is rhodopsin, a lypoprotein consisting of the chromophore 11-*cis*-retinal linked to the protein via a protonated Shiff base linkage.[1] A number of derivatives of retinal **1** have now been synthesized that examine certain structural[2] and electronic[3] features of the binding site of the chromophore within the protein. As previous attempts to form pigment from retinal derivatives not containing a ring structure have been unsuccessful,[4] it has been assumed that the ring is essential for pigment formation. We report here the synthesis of the retinal analogue **2**, which does not contain an intact ring, and the formation of a stable pigment between bovine opsin and the cis isomer of this compound corresponding to the 9-cis isomer of retinal.
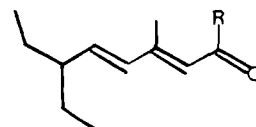
2-Ethylbutanal (Eastman) was combined with ethyl 4-(diethoxyphosphinyl)-3-methylcrotonate[5] in the presence of sodium
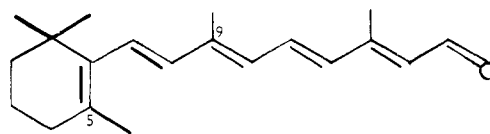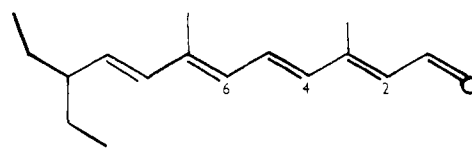
amide to yield the ester **3a** (82%). Lithium aluminum hydride reduction and manganese dioxide oxidation in ethyl ether afforded 6-ethyl-3-methyl-2,4-octadienal **3b** (45%), which was purified by preparative thin-layer chromatography (TLC). The aldehyde **3b** was condensed, reduced, and oxidized as above to yield the product 3,7-dimethyl-10-ethyl-2,4,6,8-dodecatetraenal **2** (32%). The

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Communications to the Editor

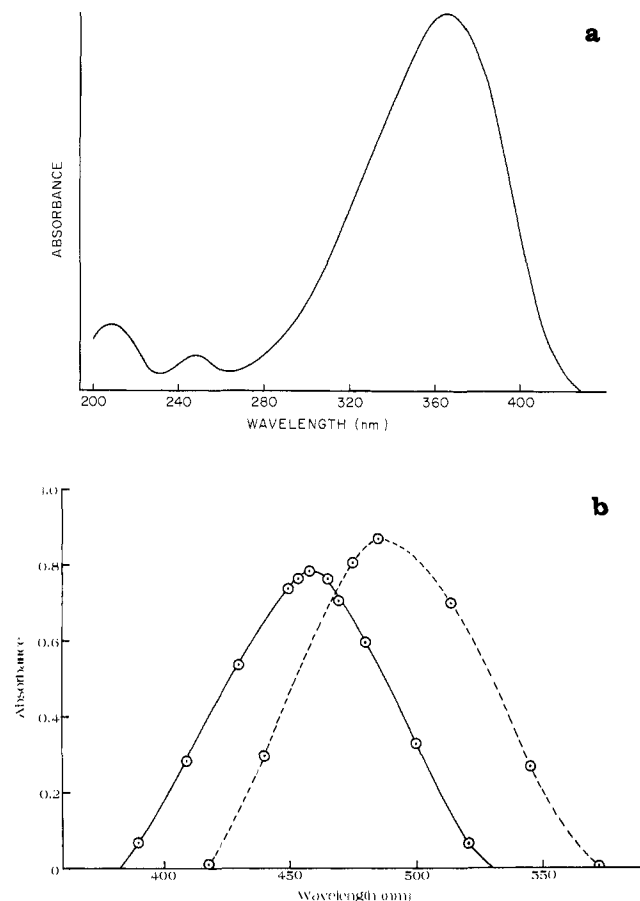*J. Am. Chem. Soc., Vol. 104, No. 18, 1982* 4947

Figure 1. (a) Absorption spectrum of 6-*cis*-3,7-dimethyl-10-ethyl-2,4,6,8-dodecatetraenal (**2**) in hexane. (b) Difference absorption spectra of pigments formed from bovine opsin and 9-*cis*-retinal (O - - - O) 6-*cis*-dimethyl-10-ethyl-2,4,7,8-dodecatetraenal (O—O). Difference spectra were obtained by substraction of the absorption spectra obtained after exposure of the pigments to light for 1 min from the spectra of the pigments before exposure (30 mm phosphate buffer, pH 7.2, 10 mm NH$_2$OH).

product was purified by TLC and high-pressure liquid chromatography (HPLC) using 1.5% ethyl ether/hexane on a μ-Porasil column. Two major isomers were obtained, both showing a parent peak in the mass spectrum at m/e 232 (70 eV). Anal. Calcd for C$_{16}$H$_{24}$O: C, 82.75; H, 10.35. Found: C, 83.01; H, 10.31. The less polar isomer on TLC and HPLC was identified as the 6-cis isomer (corresponding to the 9-*cis*-retinal isomer) by nuclear magnetic resonance spectroscopy:[6] (CDCl$_3$) δ (10.03 H-1, $J_{1,2}$ = 7.32 Hz), 0.586 (H-2), 6.23 (H-4, $J_{4,5}$ = 15.37 Hz), 7.08 (H-5, $J_{5,6}$ = 10.98 Hz), 5.95 (H-6), 6.55 (H-8, $J_{8,9}$ = 15.37 Hz), 5.54 (H-9), 1.94 (CH$_3$-3), 1.79 (CH$_3$-7). The absorption spectra (λ_{max} 360 nm, hexane, Figure 1a) is characteristic of a 5,6-dihydroretinal and is comparable to the λ_{max} of 9-*cis*-5,6-dihydroretinal (λ_{max} 364 nm, methanol).[7]

Bovine opsin was obtained from frozen retinae[8] (Hormel) and pigment regenerated with **2**. The pigment was obtained in 92% yield when compared with that of isorhodopsin regenerated from the same opsin with 9-*cis*-retinal. The pigment is stable to the addition of NH$_2$OH (10 mM) and is photobleached. The λ_{max} of the visible absorption (454 nm) of this pigment was somewhat blue shifted from that of isorhodopsin (485 nm, Figure 1b) but similar to that reported for the pigment formed from 9-*cis*-5,6-dihydroretinal (460 nm).[7] The bound chromophore was estab-
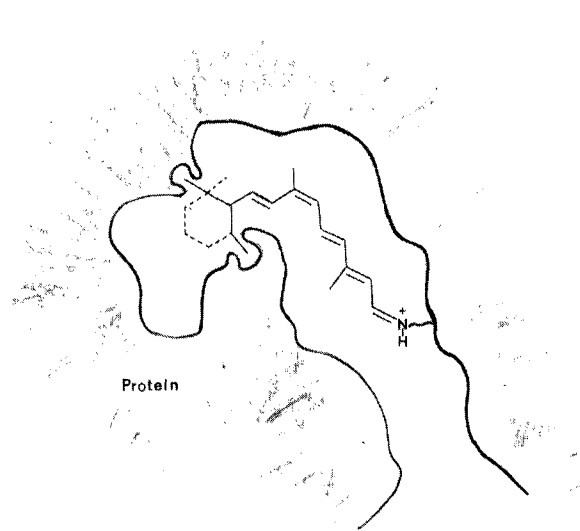
Figure 2. Schematic representation of the hypothetical interaction of the chromophore with the protein opsin. The dotted line describes the portion of retinal missing from the open-ring derivative **2**.

lished to be the 6-*cis*-3,7-dimethyl-10-ethyl-2,4,6,8-dodecatetraenal, **2**, by the CH$_2$Cl$_2$ denaturation extraction procedure.[9] The rate of pigment formation was determined by following the reaction of the 6-cis isomer of **2** with opsin, stopping the reaction at various times by the addition of NH$_2$OH, bleaching, and measuring the amount of pigment formed by difference spectra. The rate of formation of the "open ring" isorhodopsin was slower than that of isorhodopsin with a $t_{1/2}$ of 172.5 ± 3.4 s as compared with 32.9 ± 0.6 s for isorhodopsin. However, pigment formation was complete in ～15 min, whereas formation times of several hours have been reported for other synthetic pigments.[10] The pigment is stable to the addition of 9- or 11-*cis*-retinal, indicating the open-ring retinal **2** is bound to the same lysine as is retinal in native rhodopsin.

These results demonstrate that the cyclohexyl ring is not essential to the formation of a stable, photobleachable pigment derivative of bovine opsin. Our results from the study of inhibition of pigment formation with small molecules resembling portions of retinal structure have suggested the ring methyl groups are of importance for stable interaction of the chromophore with the protein.[11] At least two methyl groups, at positions equivalent to 1 and 5 on retinal, were found to be required for interaction of the small molecule with the protein and for significant inhibition of pigment formation. The synthetic retinals that are reported to form pigments, stable to hydroxylamine, in reasonable yields (<10%) with bovine opsin contain at least one methyl group on the ring. For example, no pigment is obtained with 9- and 11-cis-1,1,5-desmethyl-5,6-dihydroretinals whereas 9- and 11-*cis*-dihydroretinals form pigments in good yield under the same conditions.[7,12] Similar results have been obtained with the phenyl analogues.[10,13] The terminal methyl groups of **2** can be envisioned as filling the structural requirement for two methyl groups (Figure 2). The results from this analogue are supportive of the hypothesis that it is the ring methyl groups, rather than the ring itself, that are essential for fitting into the protein binding cavity of rhodopsin, and thus it may be the distance between these groups and carbonyl that fulfills the "longitudinal length requirements" proposed by Matsumoto and Yoshizawa.[14]

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Syntheses and Reactions of Rhenium Vinylidene and Acetylide Complexes. Unprecedented Chirality Transfer through a C≡C Triple Bond
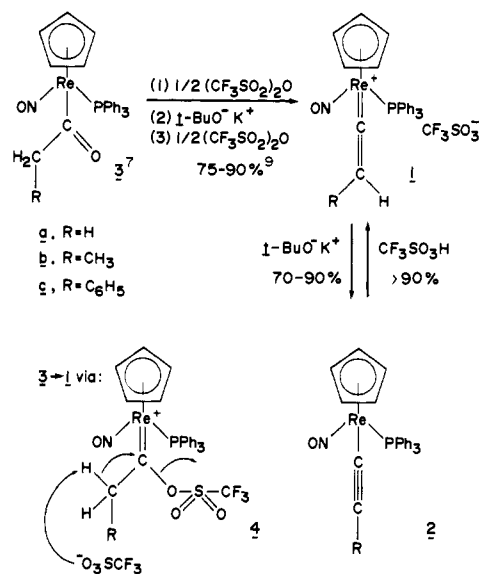
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There has been intense recent interest in the synthesis and reactivity of transition-metal alkylidene complexes (L_nM=CRR′),[2-4] vinylidene complexes (L_nM=C=CRR′)[5] and other species containing metal–carbon multiple bonds.[6] We recently described the synthesis and isolation of the pseudotetrahedral electrophilic methylidene complex [(η-C$_5$H$_5$)Re(NO)(PPh$_3$)(=CH$_2$)]$^+$PF$_6^-$ and higher Re$^+$=CHR homologues.[3,4a,d] The latter were found to exist in two photointerconvertible geometrically isomeric forms and undergo stereospecific or highly stereoselective nucleophilic attack.[4] Hence we were interested in determining if similar phenomena could be observed in metallocumulene systems, which would have the carbon π terminus more remote from the metal site. In this communication, we describe (a) the facile synthesis of chiral rhenium vinylidene and acetylide complexes [(η-C$_5$H$_5$)Re(NO)(PPh$_3$)(=C=CRR′)]$^+$X$^-$ (1) and (η-C$_5$H$_5$)Re(NO)(PPh$_3$)(C≡CR) (2) (R, R′ = H, CH$_3$, C$_6$H$_5$), (b) the first observation of geometric isomerism in vinylidene complexes, (c) the thermal and photochemical interconversion of these isomers, (d) energy barriers associated with these isomerizations, and (e) stereospecific reactions of acetylide complexes 2 that entail *transfer of the metal chirality through a C≡C triple bond of formal cylindrical symmetry*!

Vinylidene complexes **1a–c** were prepared from the corresponding rhenium acyls (**3**) by a modification of the method of

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Scheme I. Syntheses and Interconversions of Rhenium Vinylidene and Acetylide Complexes

Hughes,[5f-h] as shown in Scheme I.[7] The key step is thought to be fragmentation of the intermediate **4**. The CF$_3$SO$_3$H thus liberated protonates unreacted **3**, but this complication can be easily circumvented.[9]

The parent vinylidene [(η-C$_5$H$_5$)Re(NO)(PPh$_3$)(=C=CH$_2$)]$^+$CF$_3$SO$_3^-$ (**1a**) precipitated from CH$_2$Cl$_2$/hexane as a red powder. It exhibited *two* =CH$_2$ ^{1}H NMR resonances ((CDCl$_3$) δ 5.40, 4.94, both d, $J_{^1H-^1H'}$ = 20 Hz)[10] which did not coalesce (or undergo magnetization transfer)[11] at 110 °C (CDCl$_2$CDCl$_2$, 200 MHz). This bounds the Re$^+$=C=CH$_2$ rotational barrier, $\Delta G^{\ddagger}_{rot}$ (110 °C), as >18.6 kcal/mol. Substituted vinylidenes [(η-C$_5$H$_5$)Re(NO)(PPh$_3$)(=C=CHCH$_3$)]$^+$CF$_3$SO$_3^-$ (**1b**) and [(η-C$_5$H$_5$)Re(NO)(PPh$_3$)(=C=CHC$_6$H$_5$)]$^+$CF$_3$SO$_3^-$ (**1c**) were isolated from CH$_2$Cl$_2$ as light brown and golden crystals, respectively.[10] Both **1b** and **1c** existed in two isomeric forms (**k**, "kinetic"; **t**, "thermodynamic"; vide infra) which displayed distinct C$_5$H$_5$ and =CHR ^{1}H NMR resonances. Equilibrium ratios were (50 ± 2):(50 ± 2) (**1bk/1bt**) and (25 ± 2):(75 ± 2) (**1ck/1ct**).

Evidence was obtained that the two forms of **1b** and **1c** were *geometric* isomers that differed in the orientation of the =CHR group. First, irradiation of the (25 ± 2):(75 ± 2) **1ck/1ct** mixture (CD$_2$Cl$_2$, −78 °C, Hanovia 450-W lamp through Pyrex)[4c,d] gave a clean (50 ± 2):(50 ± 2) photostationary state. The sample was allowed to return to thermal equilibrium in the dark, and additional irradiation cycles were conducted without noticeable sample deterioration. Thus **1ck** and **1ct** can be photointerconverted analogously to C=C and Re$^+$=CHR geometric isomers.[4c,d] Second, both **1bk/1bt** and **1ck/1ct** were smoothly deprotonated by *t*-BuO$^-$K$^+$ to common products, the orange crystalline acetylides

(7) Starting acyls **3** were prepared in 65–85% yields by reaction of (η-C$_5$H$_5$)Re(NO)(PPh$_3$)(CO$_2$CH$_3$)[8] with RMgX. The physical and chemical properties of these complexes will be described in a subsequent full paper.

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(9) The first step of Scheme I yields (even with excess (CF$_3$SO$_2$)$_2$O) a 1:1 mixture of **1** and the protonated acyl [(η-C$_5$H$_5$)Re(NO)(PPh$_3$)(=C(OH)-CH$_2$R)]$^+$CF$_3$SO$_3^-$ (independently synthesized from the acyl and CF$_3$SO$_3$H). These cationic products are not separable in our hands. Addition of *t*-BuO$^-$K$^+$ deprotonates each (respectively) to a 1:1 mixture of acetylide (**2**) and **3**. Subsequent addition of (CF$_3$SO$_2$)$_2$O at −78 °C converts this mixture *entirely* to **1**, since the acetylide now acts as the base for the CF$_3$SO$_3$H liberated.

(10) Full characterization of **1a–e** and **2a–c** (^{1}H NMR, ^{13}C NMR, IR, and some mass spectral and microanalytical data) is given in the supplementary material. Selected key features include: ^{13}C NMR (ppm, CDCl$_3$) **1a–e**, 327–336 (C$_\alpha$), 113–140 (C$_\beta$), **2a–c**, 111–123 (C$_\beta$), 71–92 (C$_\alpha$); IR (cm^{-1}, CHCl$_3$) **1a–e** $\nu_{N≡O}$ 1735–1750 (s), $\nu_{C=C}$ 1645–1665 (w), **2a–c** $\nu_{N≡O}$ 1655–1658 (s), $\nu_{C≡C}$ 2020–2118 (w).

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